

REMARKS

Upon entry of the foregoing amendments, claims 1-24 are pending in the application. Claims 3, 6-9, 18, and 20-23 are withdrawn as being drawn to a non-elected invention or a non-elected species. Applicants will cancel these claims upon indication of allowable subject matter in the elected invention.

Claims 1, 13-14, 17, and 19 have been amended. Claim 24 has been added. Applicants submit that the amended claims and new claim 24 are fully supported by the specification as originally filed. No new matter has been introduced. Applicants further submit that the amendments are made merely to expedite allowance of claims directed to most commercially relevant embodiments of the present invention. Applicants reserve the right to pursue claims of similar or differing scope in the future.

Applicants now address the Examiner's rejections in the order presented in the previous Office Action dated February 12, 2004.

Election/Restriction

The Examiner has acknowledged Applicants' election, with traverse, of Group I (claims 1-17 and 19-23), and the corresponding species elections in the Response dated October 22, 2003.

Priority

Applicants note that the Examiner has acknowledged Applicants' claim for foreign priority under 35 U.S.C. 119(a)-(d).

Claim rejection under 35 U.S.C. §112, first paragraph - written description

Claims 1-2, 4-5, 10-17, and 19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, the Examiner asserts

“The specification description and examples are directed to a method of detecting ligand-binding activity (e.g. antibody-ligand or protein-protein interaction) with

known magnetic particles such as commercial beads (e.g., Dynabeads). The specification examples are drawn to an ELISA method for detecting antibody-ligand interaction with magnetic particle phage (Example 10) and a method of detecting protein-protein interaction with magnetic particle (Example 13). These methods clearly do[es] not provide an adequate representation regarding the [method] for the selection of at least one member of a number of specifically interacting molecules from libraries” (see Office Action, page 5, lines 5-15).

Applicants traverse this rejection to the extent that it is maintained in light of the amended claims for the reasons that follow. Independent claim 1 as amended recites a method for identifying from a library of molecules at least one member which specifically interacts with another molecule. The claimed method for identifying interacting molecules comprises three selection steps (a, b, and c) that are carried out in parallel in more than one container using an automated device such as a magnetic particle processor.

Contrary to the Examiner’s assertion, the selection steps of the claimed method are described in detail in the specification including working examples. For example, the specification describes that “it is to be understood that a ‘selection round’ comprises steps (a) to (c). Accordingly, the phrase ‘first step involving the contact of said interacting molecules’ denotes the contacting step of the first selection round as compared to second, third, etc. steps involving the contact of said interacting molecules of potential further selection rounds that may be performed subsequently to the first selection round (see below)” (e.g., page 5, lines 23-28).

In particular, the specification teaches that “[t]his selection involves a sequence of binding and washing steps and was adapted to high throughput using a magnetic particle processor (Labsystems, Helsinki, Finland).” Furthermore, the specification teaches that “[s]aid first and second molecule may be members of libraries, e.g., an antibody and an antigen library, respectively, i.e. two different libraries. Alternatively, said first and second molecule may be members of the same library. Also comprised by the present invention are embodiments, wherein one molecule (i.e. the first or the second molecule) is a member of a library whereas the other molecule is a compound or a variety of compounds of predetermined specificity. Other options to employ first and second molecules from still different origins or combinations of origins are within the skills of the person skilled in the art” (e.g., page 6, lines 4-15).

Applicants note that the elements of the claimed method are all well known in the art (e.g., magnetic beads, magnetic particle processors, containers, libraries, and interacting

molecules), and there is no term that would leave one of skill in the art guessing as to either its meaning or applicability to the invention. Similarly, screening and selection methods for inter-molecular interaction are routine and well known. Although this is one particular method that requires certain steps, the steps are well described in the specification and clear to one of skill in the art. Under the Guidelines for the Examination of Patent Applications Under the Written Description Requirement, 66 Fed. Reg. 1104, 1105 (Jan. 5, 2001), “[i]nformation which is well known in the art need not be described in detail in the specification.”

Furthermore, contrary to what the Examiner alleges, Applicants have demonstrated possession of the claimed invention by describing examples of actual reduction to practice of the claimed method in diverse working examples (e.g., Examples 1, 5, 8-9, and 15).

In summary, the method as recited in claim 1 is described in detail throughout the specification. Applicants have even provided several experimental measures that would have allowed one of skill in the art to readily recognize the claimed subject matter. Thus, Applicants submit that all pending claims as amended fully comply with the written description requirement. Reconsideration and withdrawal of the rejection under 35 U.S.C. 112, first paragraph, are respectfully requested.

Claim rejections under 35 U.S.C. § 112, second paragraph

Claims 1-2, 4-5, 10-17, and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Applicants traverse this rejection to the extent that it is maintained in light of the amended claims.

Specifically, the Examiner asserts that “[i]t is not clear as to the correlation of the term ‘libraries’ of claim 1 with regard to the claimed method steps since the claimed method steps refers to the method of detecting interaction between the first and second molecules.”

Applicants respectfully disagree. As described above, the specification teaches that “[s]aid first and second molecule may be members of libraries, e.g., an antibody and an antigen library, respectively, i.e. two different libraries. Alternatively, said first and second molecule may be members of the same library. Also comprised by the present invention are embodiments, wherein one molecule (i.e. the first or the second molecule) is a member of a library whereas the

other molecule is a compound or a variety of compounds of predetermined specificity” (e.g., page 6, lines 8-13). Thus, in view of the above teachings, one of skill in the art would know the correlation of the term “libraries” of claim 1 with regard to the claimed method steps.

Nevertheless, solely to expedite prosecution, Applicants have amended claim 1 to clarify the claimed invention. In addition, Applicants have added claim 24 to specify that the second molecule is in a library of molecules. Applicants submit that these claim amendments are fully supported by the specification (e.g., page 6, lines 8-13).

The Examiner further asserts that “[t]he method step (d) is vague and indefinite because it is unclear as to the ‘providing the first and/or second molecule selected by steps (a) to (c)’ when the result of steps (a) to (c) is the product of the ‘compound/composition’ of the interaction of the first and second molecules.”

Solely to expedite prosecution, Applicants have amended claim 1 to clarify the claimed method. As amended, step (d) of claim 1 recites “determining the identity of said first and/or second molecule selected by steps (a) to (c).” Applicants submit that methods for determining the identity of a molecule (e.g., a nucleic acid or a polypeptide) are routine and well known in the art. For example, the specification teaches that “[m]ethods for the characterization of genetic information, i.e. nucleic acids, and proteinaceous material are well known in the art and include, e.g., nucleic acid sequencing, southern-, northern-, and colony hybridization, primer extension analysis, RNase protection assay, gel shift analysis, western-blotting, ELISA, immunoprecipitation assay, indirect immunofluorescence analysis, and FACS” (e.g., page 8, lines 20-24). Alternatively, the identity of a molecule (e.g., a known molecule) may be ascertainable by other standard methods, such as by checking the location of a well against a known structure that is recorded and predetermined as having been added to that well.

The Examiner also asserts that “the second limitation of ‘and, if said specific interaction had occurred’ of step (c) of claim 1 is vague and indefinite because it is a reiteration of the first limitation of ‘determining whether a specific interaction between said first and second molecule had occurred.’”

Solely to expedite prosecution, Applicants have amended step (c) of claim 1, which recites “selecting said first molecule and second molecule which specifically interact.”

Applicants submit that one of skill in the art would understand step (c) of the claimed method, particular in view of the working examples (e.g., Example 15) in the specification.

The Examiner further asserts that “the term ‘specific interaction’ of claim 1 is a relative term, which renders the claim indefinite.”

Applicants respectfully disagree. The term “specific interaction,” when read in a biological context, is completely clear for one skilled in the art. Generally, the interaction occurs only between the two interacting partners. In another word, the interaction does not occur if one of the partners is substituted by a different molecule. Nevertheless, Applicants have amended claim 1 to clarify the claimed invention.

The Examiner further asserts that claim 17 is vague and indefinite because its limitation is synonymous to the limitation of claim 1 step (d). Solely to expedite prosecution, Applicants have amended claims 1 and 17 such that the limitation of claim 1 is not repeated in claim 17.

The Examiner asserts that there is insufficient antecedent basis for the limitation “second molecule target” in claim 13. Applicants have amended claim 13 to overcome the rejection.

The Examiner further asserts that claims 1-2, 4-5, 10-17, and 19 are incomplete for omitting essential steps. The alleged omitted steps are the step(s) of “selecting” a member of a number of specifically interacting molecules from libraries. As described above, Applicants have amended independent claim 1 to clarify the “selecting” step in the claimed method.

Based on the amendments and arguments presented above, Applicants submit that all claims as amended comply with the requirement of 35 U.S.C. 112, second paragraph. Therefore, reconsideration and withdrawal of rejections under 35 U.S.C. 112, second paragraph, are respectfully requested.

Claim rejections under 35 U.S.C. § 102:

Claims 1-2, 4-5, 10-13, 15-17, and 19 are rejected under 35 U.S.C. 102(b) as allegedly being anticipated by McConnell et al. Claims 1-2, 10-13, and 15-17 are rejected under 35 U.S.C. 102(b) as allegedly being anticipated by Kausch et al. Claims 1-2, 4, 10-13, and 15-16 are rejected under 35 U.S.C. 102(b) as allegedly being anticipated by Chagnon et al. Claims 1-2, 10-17, and 19 are rejected under 35 U.S.C. 102(b) as allegedly being anticipated by Neurath et al.

Claims 1-2, 4-5, 10-17, and 19 are rejected under 35 U.S.C. 102(a) as allegedly being anticipated by Wang et al. Applicants traverse the rejection to the extent that it is maintained in light of the amended claims.

The standard for anticipating a claim is clearly outlined in MPEP 2131, and this standard is further supported by the Courts. “A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.” *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1978). “The identical invention must be shown in as complete detail as is contained in the claim.” *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989).

Applicants contend that these cited prior art references, singly or in combination, fail to satisfy this criteria for anticipating the present invention.

McConnell et al. mainly describe a study for clarifying which surfaces, planar microtitre plate wells or round paramagnetic particles, are better for selecting phage displayed molecules. The present invention is directed to novel methods that comprise moving the paramagnetic beads from the individual solution in the selection steps. In contrast, McConnell et al. disclose a method wherein all selection steps are performed in the same vial. Moreover, Applicants submit that nitrocellulose filter assays described by McConnell et al. are not arrays in the sense of linking the phenotypic and genotypic information. As a skilled artisan would know, the individual binders are not in the same position when reproducing the experiment with nitrocellulose filter assays, and hence their identity is not linked to the position. Accordingly, Applicants respectfully submit that McConnell et al. fail to teach or suggest each and every limitation of the present claims, and thus fail to anticipate the claimed subject matter.

Kausch et al. describe a method for isolating interacting partners using magnetic particles. The method of Kausch et al. is essentially a purification process (as opposed to an *identification* process) because the interacting partners were known to interact with each other when the method was performed, and it was for this reason that the method was selected for separating the compounds. For example, Kausch et al. teach that the affinity ligand affixed to the magnetic particles is known to bind to chromosomes. Thus, Kausch teach a method for purification purposes and not for the identification and selection of novel binding partners. In

contrast, the present invention is directed to methods for identifying and selecting interacting molecules that are not known to interact with each other. The claimed method comprises “determining the identity” of the interacting molecules, which is not described or suggested by Kausch et al. Accordingly, Applicants respectfully submit that Kausch et al. fail to teach or suggest each and every limitation of the present claims, and thus fail to anticipate the claimed subject matter.

Chagnon et al. describe a binding assay using magnetic particles. Similarly, the assay of Chagnon et al. is essentially a purification process because the binding assay was performed on molecules that were known to interact with each other. As described above, the present invention is directed to methods for identifying and selecting interacting molecules that are not known to interact with each other. The claimed method comprises “determining the identity” of the interacting molecules, which is not described or suggested by Chagnon et al. Accordingly, Applicants respectfully submit that Chagnon et al. fail to teach or suggest each and every limitation of the present claims, and thus fail to anticipate the claimed subject matter.

Neurath et al. describe a screening method for identifying a test compound that inhibits binding of a ligand to a receptor. Neurath et al. do not teach a method for identifying and selecting interacting molecules from a library as recited in the present invention. Moreover, Applicants submit that the magnetic particles and the magnetic separator are used only to hold the cells in place in the microtitre plate (MTP), not to move the beads in an automated fashion from container to container as recited in the pending claims. In addition, Applicants point out that the separator described by Neurath et al. is not an automated (e.g., controllable) device for movement as recited in the present invention, but merely a strong magnet in microtitre plate format manually placed under the MTP. Accordingly, Applicants respectfully submit that Neurath et al. fail to teach or suggest each and every limitation of the present claims, and thus fail to anticipate the claimed subject matter.

Wang at al. describe a screening method and device, wherein the identity of a first molecule is known due to its predetermined position (e.g., on an array). The array is incubated with a complex solution of labeled molecules, and bound molecules are detected with a laser-scanning device. However, the magnetic beads used by Wang at al. are solely used to obtain defined particles of the first molecule which can then be held in defined positions on the array by

a magnet. Hence, holding the magnetic particle in place is crucial for obtaining a predetermined array and the system does not allow any transfer of the magnetic particles by any means. In contrast, in the claimed invention, the magnetic particles are transferred to a new container in an automated fashion. Accordingly, Applicants respectfully submit that Wang et al. fail to teach or suggest each and every limitation of the present claims, and thus fail to anticipate the claimed subject matter.

Accordingly, Applicants respectfully submit that the cited references, taken alone or in combination, fail to meet the limitations of the present claims and thus fail to anticipate the claimed subject matter. Reconsideration and withdrawal of this rejection are respectfully requested.

In addition, Applicants point out that the cited prior art references, taken alone or in combination, do not teach or suggest a method which allows for identifying and selecting molecules unknown to interact with each other and requires transferring magnetic particles from one container to another container in an automated fashion. One of ordinary skill in the art would not have been motivated to adapt the teachings of any of the cited references to arrive at a method as claimed in the present invention, and could have had no reasonable expectation of success in practicing the present invention. Accordingly, Applicants submit that the pending claims as amended are nonobvious because the cited prior art references, taken alone or in combination, fail to establish a *prima facie* case of obviousness.

CONCLUSION

The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000. Should an extension of time be required, Applicants hereby petition for same and request that the extension fee and any other fee required for timely consideration of this submission be charged to **Deposit Account No. 18-1945**.

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Customer No: 28120
Docketing Specialist
Ropes & Gray LLP
One International Place
Boston, MA 02110
Phone: 617-951-7000
Fax: 617-951-7050

Respectfully Submitted,



David P. Halstead, Ph.D.
Reg. No. 44,735